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## Syphilis

Syphilis is a chronic infectious disease that is almost entirely transmitted by direct intimate contact with the infectious lesions of early syphilis, and also from an infected mother to her infant before or at the time of birth. It is systemic from the onset and capable of involving any structure of the body. If left untreated, it progresses through stages: primary, secondary, latent, and late syphilis (tertiary).

**A. Etiologic Agent:** *Treponema pallidum*: a spirochete

**B. Mode of Transmission:** Sexual contact (vaginal, oral, and anal sex) and also from an infected mother to her infant before or at the time of birth. Although it is technically possible to transmit syphilis through other intimate contact, it is extremely unlikely. For spread to occur, susceptible tissue must come into direct contact with infectious lesions in the primary and secondary stages.

Sexual abuse must be suspected in any young child with acquired syphilis. (2000 Red Book, p.548)


Infections that . . . . can be asymptomatic for long periods after vertical transmission (e.g., syphilis . . . .) are more problematic [in terms of assessing the likelihood of sexual abuse]. The possibility of vertical transmission should be considered in these cases, but an evaluation of the patient's circumstances by the local child protective services agency is warranted in most. (2000 Red Book, p.143)

**C. Clinical picture:**

Syphilis is a systemic infection caused by *Treponema pallidum*.

Primary syphilis is characterized by one or more painless, superficial ulcerations (chancres) at the site of exposure. Such lesions may be seen at any site in the genital, anorectal, or oropharyngeal tracts; thus a high index of provider suspicion is required when any patient presents with a mucosal ulcer or "sore." The chancre often has raised, sharply demarcated borders, a red smooth base, and scanty serous secretion, although the clinical presentation is quite variable, Regional lymphadenopathy may also be present. Average time from infectious exposure to lesion development is three weeks (range 9-90 days). Resolution of lesions generally occurs three to six weeks thereafter without treatment.

Secondary syphilis may develop following resolution of primary lesions. Secondary disease is characterized by macular, maculopapular, or papular skin lesions ("rash"), typically involving palms, soles and flexor areas of the extremities. The trunk, back, shoulders, abdomen and face are also commonly involved. Pustular lesions and condylomata lata may infrequently occur. Average time from infectious exposure to onset of secondary symptoms is six weeks.

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Latent syphilis is diagnosed serologically in the absence of primary or secondary clinical signs. Early disease ( $\leq 1$  year) is differentiated from late disease ( $> 1$  year) for treatment purposes (see below). **If a negative serology within the past year cannot be documented or an epi-link cannot be identified, patients should be treated for late latent disease.**

Tertiary syphilis is rare, but may manifest as mucocutaneous/osseous lesions (gummas), cardiovascular lesions (aortitis), or neurologic involvement (neurosyphilis). While neurosyphilis is generally a late complication of infection, syphilitic meningitis may occur as an early complication within the first few weeks of infection, or at any time thereafter.

#### D. Diagnosis:

1. Darkfield microscopy of lesion exudate: specific but insensitive
2. Non-treponemal serologic test: RPR (Rapid Plasma Reagin) **or** VDRL (Venereal Disease Research Laboratory)
  - a. Often reactive within one to two weeks of chancre onset
  - b. Up to 30% may have **negative** RPR at time of initial exam.
  - c. False-positive in variety of conditions
  - d. False-negative prozone effect in 1-2% of secondary syphilis; serum is reactive with serial dilutions
  - e. RPR generally runs approximately 1 titer higher than VDRL; both tests are only accurate to within  $\pm 1$  dilution
3. Treponemal serologic test to confirm infection: FTA-ABS (fluorescent treponemal antibody absorption), MHA-TP (microhemagglutination assay for *T. pallidum*), **or** TP-PA (*Treponema pallidum*-Particle Agglutination)
4. Newer tests, such as direct fluorescent antibody (DFA) examination of lesion exudate, are not widely available

**E. Differential Diagnosis:** Early syphilis should be included or excluded in the management of patients with genital, anal or oral lesions; or skin or body rash. Other genital ulcer diseases include herpes, chancroid, and lymphogranuloma venereum.

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**F. Treatment:** See CDC STD Treatment Guidelines in the appendix or online at:

[www.cdc.gov/std/treatment/default.htm](http://www.cdc.gov/std/treatment/default.htm)

Jarisch-Herxheimer reaction

- a. Systemic manifestations of treponeme lysis: release of treponemal constituents, presumably in an endotoxin-like reaction.
- b. More common in early syphilis
- c. Fever, malaise, headache, musculoskeletal pain, nausea, tachycardia may occur within four to eight hours of treatment, resolve within 24 hours
- d. Not dependent on type or dose of antibiotic used, should not be mistaken for a penicillin reaction
- e. Not an indication for discontinuation of treatment; most reactions can be managed by reassurance of patient and fluids, acetaminophen, ibuprofen as needed

**NOTE: For all stages of syphilis, penicillin is the treatment of choice.** If doxycycline or any other antibiotic is given, stress adherence to the regimen since deletion of only a few doses significantly increases the failure rate. For pregnant patients with history of true penicillin allergy, penicillin skin testing and desensitization are required, since alternative medications do not treat the fetus.


## **G. Follow Up of Reactive Serologic Tests for Syphilis (STS)**

Because non-treponemal antibodies may persist in treated patients (known as Wasserman-fast or serofast patients), the reactive serology will be researched in the central registry of the disease intervention program. The registry consists of previously reported reactive syphilis lab reports and epidemiological investigation outcomes, including diagnosis or biologic false positive (BFP) information.

## **H. Sex partners**

Refer all patients with syphilis to your regional Disease Intervention Specialist (see Section 1, Sexually Transmitted Disease Intervention Program) for immediate counseling and interview. All partners with potential exposure must be referred for clinical evaluation. Notify STD Intervention Program staff before examining and treating contacts to discuss contact history and appropriate management. In general, the following guidelines apply:

1. Partners of patients with early syphilis ( $\leq 1$  yr. duration)
  - a. Routine history, examination, and serologies (syphilis, HIV)
  - b. Routine epidemiologic treatment for **all partners within the preceding 90 days**, regardless of serologic test result
  - c. Treat partners  $>90$  days if test results not immediately available or follow-up cannot be assured.

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2. Partners of patients with late syphilis (>1 yr. duration)
  - a. Routine history, examination, and serologies (syphilis, HIV)
  - b. Obtain specific treponemal test (MHA-TP, TP-PA)


The time periods before treatment used for identifying at-risk sex partners are:

- a. Three months plus duration of symptoms for primary syphilis;
- b. Six months plus duration of symptoms for secondary syphilis; and
- c. One year for early latent syphilis.

**I. Patient Education:** STD education should be an integral part of early syphilis management. The patient should be provided information on the clinical stages of syphilis. The patient should be encouraged to assist the Disease Intervention Program staff in locating and informing all sexual contacts and others at high risk for this infection. Syphilis is a serious disease with potentially grave consequences if the infected person is not adequately treated. The patient will be provided information to help ensure adequate treatment and follow-up.

#### **J. Other management issues**

1. Follow-up after treatment
  - a. Early syphilis
    - i. Clinical examination and repeat serology at six and 12 months, or sooner if clinically indicated
      - a. RPR should show a 4-fold titer decrease within six months of treatment
      - b. Use same test at each visit to facilitate interpretations, since RPR titers are often slightly higher than VDRL
    - ii. Consider treatment failure vs. reinfection if signs or symptoms persist or recur, or if non-treponemal titer increases 4-fold – lumbar puncture (LP) generally indicated before retreatment unless reinfection is certain
    - iii. If HIV-negative (or if not tested), advise repeat HIV testing at three to six months
  - b. Late syphilis
    - i. Repeat serology in 6, 12, and 24 months
    - ii. Evaluate for neurosyphilis if:
      - a. non-treponemal titer increases 4-fold
      - b. initially higher titer ( $\geq 1:32$ ) fails to fall 4-fold in 12-24 months
      - c. signs or symptoms of syphilis development
  - c. Neurosyphilis
    - i. Repeat serology in 3, 6, 12, and 24 months
    - ii. Follow-up lumbar puncture (LP) at six-month intervals until cell count is normal
    - iii. Consider retreatment if cell count not decreased at six months or CSF not entirely normal at two years
  - d. Syphilis (any stage) in HIV-positive patients


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- i. Clinical examination in one week
  - ii. Repeat serology in 3, 6, 9, 12, and 24 months, then yearly (even if RPR becomes negative)
2. Indications for lumbar puncture (LP) in latent syphilis
  - a. Neurologic or ophthalmic signs/symptoms
  - b. Evidence of tertiary disease (gumma, aortitis, iritis)
  - c. Treatment failure
  - d. HIV infection
    - i. HIV+ early latent syphilis does not need routine LP unless clinically indicated
    - ii. Close follow-up required, since up to 25% of HIV+ patients may develop neurosyphilis despite adequate therapy

NOTE: Common exceptions to LP include:

- asymptomatic elderly patients with late latent syphilis, RPR  $\leq$  1:4
- Patients with RPR  $\leq$  1:2 for whom the probable duration since primary infection is  $\geq$  30 years
- immigrants from geographic areas with high prevalence of pinta or yaws (e.g. the tropical Americas, Southeast Asia, Central Africa) who have no history of prior syphilis and RPR  $\leq$  1:4

3. Syphilis during pregnancy
  - a. Recommend all women should be screened serologically in first trimester. For high risk women, additional testing should occur in the third trimester and at delivery  
Missouri [statute 210.030](#) states that a pregnant woman in the state of Missouri shall, if the woman consents, be tested for syphilis at the time of the first prenatal examination, or not later than twenty days after the first prenatal examination. In any area of the state designated as a syphilis outbreak area by the Department of Health and Senior Services, if the mother consents, a sample of her venous blood shall be taken later in the course of pregnancy and at delivery for additional testing for syphilis.
  - b. Treat with the penicillin regimen appropriate for the stage of disease
  - c. Some experts give **one additional dose** of benzathine PCN IM one week after the initial dose for patients with early syphilis during pregnancy
  - d. Advise patients treated in second half of pregnancy about Jarisch-Herxheimer reaction, which can precipitate premature labor, fetal distress
  - e. True penicillin allergy in pregnant woman requires skin testing and desensitization, since alternative medications do not treat the fetus

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## **Websites**

DHSS Disease Directory: Syphilis

<http://www.dhss.state.mo.us/GLRequest/ID/SyphilisE.html>

CDC: Syphilis Fact Sheet

<http://www.cdc.gov/stopsyphilis/SyphilisFact.htm>

NIAID. Syphilis

<http://www.niaid.nih.gov/factsheets/stdsyph.htm>

National Network of STD/HIV Prevention Training Centers (PTCs).

Curriculum Outline: Clinical STD Training Courses: Syphilis

<http://depts.washington.edu/nnptc/>